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Questions and answers

Withdrawal of the marketing authorisation application for Emerflu [pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)]

On 1 December 2010, Sanofi Pasteur SA officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Emerflu, for the prevention of 'pandemic' flu.

What is Emerflu?

Emerflu is a vaccine. It is a suspension for injection that contains parts of influenza (flu) viruses that have been inactivated (killed). Emerflu contains a flu strain called 'A/Vietnam/1194/2004 NIBRG 14' (H5N1).

What was Emerflu expected to be used for?

Emerflu was expected to be used in adults to protect against 'pandemic' flu. It was only intended for use once a flu pandemic had been officially declared. A flu pandemic happens when a new type (strain) of flu virus appears that can spread easily from person to person because people have no immunity (protection) against it. A pandemic can affect most countries and regions around the world.

How was Emerflu expected to work?

Emerflu was expected to work as a 'mock-up' vaccine. This is a special type of vaccine that is designed to help with the management of a pandemic.

Before a pandemic starts, nobody knows which strain of flu virus will be involved, so pharmaceutical companies cannot prepare the correct vaccine in advance. Instead, they can prepare a vaccine that contains a strain of flu virus specifically chosen because nobody has been exposed to it, and to which

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7129
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

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nobody is immune. They can then test this vaccine to see how people react to it, allowing them to predict how people will react when the flu strain causing the pandemic is included.

Vaccines work by 'teaching' the immune system (the body's natural defences) how to defend itself against a disease. Emerflu contains small amounts of haemagglutinins (proteins from the surface) of a virus called H5N1. The virus has first been inactivated so that it does not cause any disease. If a pandemic were to start, the virus strain in Emerflu would have been replaced by the strain causing the pandemic before the vaccine could have been used.

When a person is given the vaccine, the immune system recognises the virus as 'foreign' and makes antibodies against it. The immune system is then able to produce antibodies more quickly when it is exposed to the virus again. This is expected to help to protect against the disease caused by the virus. The vaccine also contains an 'adjuvant' (a compound containing aluminium), which is expected to stimulate a better response.

What did the company present to support its application?

The effects of Emerflu were first tested in experimental models before being studied in humans.

The main study of Emerflu included 600 healthy adults and compared the ability of two doses of Emerflu, to trigger the production of antibodies ('immunogenicity'). The participants received two injections of Emerflu containing one of two different doses of haemagglutinin. The higher dose vaccine also contained the adjuvant. The injections were given 21 days apart. The main measure of effectiveness was the level of antibodies against the flu virus in the blood at three different times: before vaccination, on the day of the second injection (day 21) and 21 days later (day 42).

In addition, 100 further people received Emerflu that contained a different strain of flu virus. Some of the participants in the studies of Emerflu went on to receive a third dose of the vaccine, containing either of the two flu virus strains, with or without the adjuvant.

How far into the evaluation was the application when it was withdrawn?

The evaluation had finished and the CHMP had given a negative opinion. The company withdrew before the European Commission had issued a decision on this opinion.

What was the recommendation of the CHMP at that time?

The CHMP was concerned over the ability of Emerflu to trigger the production of enough antibodies against the flu virus. According to criteria laid down by the CHMP, a mock-up vaccine needs to bring about protective levels of antibodies in at least 70% of people for it to be considered suitable. Because antibody production following Emerflu administration was below this level in the main studies (less than 40% in participants aged below 60 years), the CHMP was concerned that Emerflu was not suitable for use as a mock-up vaccine.

Similar results were seen in the people who received Emerflu that contained a different strain of flu virus, and there were contradictory results in the studies looking at the effects of a third dose of Emerflu. Therefore, the Committee was also concerned that the vaccine's immunogenicity was low, regardless of the strain of virus included, and that the vaccine might not be able to adequately prepare the immune system for future infections.

At that point in time, the CHMP was of the opinion that the benefits of Emerflu used for prophylaxis of influenza in an officially declared pandemic situation did not outweigh its risks. Hence, the CHMP recommended that Emerflu be refused marketing authorisation.

What were the reasons given by the company for withdrawing the application?

The letter from the company notifying the Agency of the withdrawal of the application is available under the tab ‘All documents’.

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that, at the time of the withdrawal, there were no clinical trials being carried out with Emerflu.